REMARKS

Status of the claims

Claims 1 and 26 have been amended; claim 17 has been canceled, and its limitations amended into claim 1. Claims 15, 16, and 20-23 have been canceled. All canceled subject matter is without prejudice to the prosecution of the subject matter in this or a continuing application.

Support for the amended claims can be found, inter alia, as follows:

Claim 1: page 3, lines 17-28, and claims 2, 4, 6, 8, and 17 as originally filed.

Claim 26: page 20, lines 15-16.

No new matter has been added.

Claims 1, 8-11, 18, 19, and 24-26 are currently pending.

Objections to the Drawings

The Office objected to the drawing because they lacked sequence identifiers. Applicants respectfully submit replacement drawings for all Figures, which have been reformatted for easier reading, labeled more clearly, and include the missing sequence identifiers. The replacement drawings add no new matter. Applicants respectfully request the replacement drawings be entered.

The claims are definite and enabled (35 USC 112)

The Office has rejected claims 1, 8-11 and 15-26 for being indefinite. Applicants have obviated the rejection by amendment. First, Applicants have cancelled claims 15-17 and 20-23. Secondly, Applicants have amended claim 1 to: (1) specify the cells; (2) clarify the biologically active compound, (3) clarify "increase," and (4) delete "in part" from modifying "methyl malonyl CoA."

The amendments obviate the Office's enablement rejection of these same claims. Applicants therefore respectfully request the Office to withdraw its rejections based on 35 USC 112.

The claims are novel (35 USC 102)

The Office has rejected claims 1, 8-11, 15-17 and 19-26 as being anticipated by Vrijbloed et al. (*J. Bacteriol.* 181:5600-5 (1999); "Vrijbloed") under 35 USC 102(b). Applicants respectfully traverse. Vrijbloed fails to teach each and every limitation of the rejected claims because Vrijbloed does not show an increase in the production of a biological compound derived from methyl malonyl CoA that results from inhibiting an activity of methylmalonyl coenzyme A mutase ("MCM").

The Office asserts that Vrijbloed "disclose insertional inactivation of methylmalonyl coenzyme A (CoA) mutase and isobutyryl-CoA mutase genes in *Streptomyces cinnamonensis*, which influence on [sic.] enhanced polyketide antibiotic biosynthesis." The Office does not point to anywhere in Vrijbloed to support its claim; and indeed, it cannot, because Vrijbloed did not report this result.

Vrijbloed created a MCM mutant by insertional mutagenesis that targeted the *mutB* gene (p. 5601, column 2, first paragraph of "Results"). In characterizing the mutant's phenotype, Vrijbloed grew the mutant on various media. First, Vrijbloed grew the mutant on solid minimal media containing single carbon sources, which results are reported in Table 2 (p. 5601, column 2, "Phenotype analysis fo the *S. cinnamonensis* mutant strains"). Table 2 reports on the vigor of mycelial growth on the different single carbon-source media. Production of monensin is not mentioned. Vrijbloed then grew the mutant and wild-type in a complex, oil-based medium and reported on monensin A production, observing that production by both mutant and wild-type was produced at "comparable levels" (p. 5602, first column, lines 2-3). Vrijbloed then reports that the mutant, when grown in chemically defined medium, grew equally well as wild-type (p. 5602, column 1, last sentence of first paragraph). The remaining experiments examined the incorporation of ^{13}C-labeled precursors into monensin by the mutant strains (p. 5602, "Incorporation of ^{13}C-labeled precursors into monensin A" section). Vrijbloed never reports further on monensin levels by the mutant.

No where does Vrijbloed report that the *mutB* insertional mutant produced greater levels of monensin A or any other biologically active compound derived from methylmalonyl-CoA. According to Vrijbloed's observations, the mutant produced only comparable levels of monensin.

Vrijbloed does not anticipate that rejected claims because Vrijbloed does not disclose an increase in a biologically active compound derived from methylmalonyl-CoA that results from the inhibiting an activity of MCM. Applicants respectfully request the Office to withdraw the rejection.

The claims are non-obvious (35 USC 103)

The Office has rejected claim 18 as obvious in view of Vrijbloed (supra) and Katz et al. (*Med Res Rev* 19:543-58 (1999); "Katz"). Applicants respectfully traverse. Vrijbloed teaches away from increasing a biologically active compound derived from methylmalonyl-CoA by inhibiting an activity of methylmalonyl-CoA mutase; Katz fails to remedy Vrijbloed's deficiency.

As discussed above, Vrijbloed never reports further on monensin levels by the mutant other than to indicate that the MCM mutant produced comparable levels of monensin A as the wild-type. No where does Vrijbloed report that the *mutB* insertional mutant produced greater levels of monensin A or any other biologically active compound derived from methylmalonyl-CoA. According to Vrijbloed's observations, the mutant produced comparable levels of monensin.

Vrijbloed manipulated the MCM gene in *Streptomyces cinnamonensis*, but did not manipulate the same gene in either *Saccharopolyspora* or *Aeromicrobium*.

Katz is a review article directed to engineering macrolides via genetic engineering of polyketide synthases. The Office has cited Katz as suggesting MCM manipulation in *Saccharopolyspora*. Katz does not teaching any manipulation of biologically active compounds derived from methylmalonyl-CoA by manipulating MCM.

One of skill in the art would not have any reasonable expectation of success by combining the teachings of Vrijbloed with those of Katz to increase the production of a biologically active compound derived from methylmalonyl-CoA by inhibiting an activity of MCM for the following reasons. First, Vrijbloed teaches away from doing so, because Vrijbloed's insertional MCM mutant did not increase production of monensin, a biologically active compound derived from methylmalonyl-CoA. Secondly, one of skill in the art would have no reasonable expectation of success of increasing a biologically active compound derived from methylmalonyl-CoA by inhibiting an activity of MCM by combining the teachings of Katz and the teachings of Vrijbloed because Katz fails to rectify Vrijbloed's deficiencies. Applicants respectfully request the rejections to be withdrawn.

REQUEST FOR RECONSIDERATION

Applicants believe the claims are in condition for allowance. Such action is respectfully requested. In any case, Applicants eagerly await an action on the merits.

If a telephone call would expedite allowance of the application in any form, the Examiner is invited to contact the undersigned.

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Respectfully submitted,

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